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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/062,623	BOROVSKY ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/21/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70* is/are pending in the application.

4a) Of the above claim(s) *11-13 and 65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,14-64 and 66-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application filed January 31, 2002, is a continuation in part of application 09/295,849, filed April 21, 1999, now abandoned.

Election/Restriction

Applicant's election of Group II, claims 1-10, 14-64, 66-70, drawn to methods and compositions for pest control wherein NPF peptides are administered to pests via recombinant cells expressing the peptides with traverse is acknowledged. It is noted that Applicants have not provided any arguments in the traversal. Therefore, absent any arguments the restriction requirement is maintained for the reasons of record. Claims 11-13 and 65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

In addition, Applicants have elected SEQ ID NO: 9 as an elected species. Upon review of the disclosure, it would not be considered an undue burden to examine the genus of NPF peptides taught in the specification. Therefore, the election of a species of NPF polypeptide is withdrawn.

Claims 1-10, 14-64, 66-70 as they are drawn to a method of controlling a pest comprising administering a cell which produces an effective amount of a NPF peptide and methods of making are currently under examination.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). 37 CFR 1.821(d) states: "[w]here the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description of claims, even if the sequence is also embedded in the text or the description or claims of the patent application. Specifically, the specification contains sequences not identified by SEQ ID NOs. See for example page 4, end paragraph 0011.

Appropriate correction is required.

The absence of proper sequence listing did not preclude the examination on the merits however, **for a complete response to this office action, applicant must submit the required material for sequence compliance.**

Claim Objections

Generic claims 1-10, 14-64, 66-70 are objected to because their scope has not been amended in accordance with the elected subject matter drawn to methods and compositions for pest control wherein NPF peptides are administered to pest via recombinant cells expressing the peptides.

Claims 1-3, 5-9, 13-54, 58-61, and 63-67 are objected to because of the following informalities: The form of the claims is objected since each claim must be the object of a sentence starting with "I (or we) claim", "The invention claimed is" (or equivalent). See MPEP § 608.01(m).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 14-64, 66-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are broadly drawn to compositions and methods comprising "NPF polypeptides" or "functional equivalents thereof". Neither the term "NPF polypeptide" nor "functional equivalents thereof " are adequately described in the specification. Without a clear description of an NPF polypeptide, one cannot design a polynucleotide encoding an NPF polypeptide. Moreover, providing a written description of a polypeptide or polynucleotide in terms of the biological properties conferred thereof is particularly problematic in view of the fact

that the specification does not clearly define what function is being referred to in the term "functional equivalent" or "functional equivalent thereof". An adequate written description of "NPF polypeptides" or "functional equivalents thereof" requires more than a mere statement that it is part of the invention or reference to a potential method for isolating it; what is required is a specific description of the compositions as they actually exist. It is not sufficient to define compositions or methods solely by their principal biological property, i.e. "comprising a polynucleotide encoding an NPF polypeptide and/or a functional equivalent thereof" or size (e.g. having a 2-5 amino acid segment of the amino acid sequence) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any all compositions and/or methods comprising that biological property. Naming a type of material generically known or thought to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a nucleic acid encoding any member of the NPF polypeptide genus, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the cells and/or nucleic acids have been isolated. Thus, claiming all cells or polynucleotides that comprise a function without defining the means for obtaining these are not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CA FC, 1991); *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993); and *Regents of the Univ.*

Calif. v. Eli Lilly & Co., 43 USPQ2d 1398 (CA FC, 1997)). Adequate description of the materials or methods first requires an adequate description of the materials, i.e. specific polynucleotides or cells comprising such, which provide the means for practicing the invention.

Claims 1-10, 14-64, 66-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining enablement are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation....Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Factors that can be used in evaluating undue experimentation include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

The subject invention pertains to compositions and methods for controlling pests comprising the use of polynucleotides encoding an NPF polypeptide and/or a functional equivalent thereof. The specification fails to provide an adequate guidance on *how to make* the broad range of embodiments encompassed by the recited claims, because it does not clearly define the minimal structure or consensus core structure that defines the genus comprising NPF polypeptides and because it does not provide adequate guidance describing what a functional equivalent of an NPF polypeptide is. At the time this application was filed, Cerstiaens et al. (Peptides, 20:(1):39-44, 1999) reported on a class of peptides, the "FMRFamide-related peptides (FaRPs) of insects, that appears to represent a similar class of peptides to those referred to in the instant invention (i.e. NPF polypeptides), including two represented by SEQ ID NOs:1 and 2 of the instant application and described by Cerstiaens as "two NPY-like (NPFs) from the Colorado potato beetle [that] can be added to this ever expanding number of N-terminally extended RFamides" (sentence abridging left and right columns of p. 39). Cerstiaens characterized the prior art wherein the "immunohistochemical results *suggest a possible role in insect reproduction* for peptides of the superfamily of the FaRPs. Yet, no effect *in vivo* from members of this extended family of peptides has been reported as yet" (p. 40, middle, left column). One cannot make a polynucleotide encoding an NPF polypeptide if it cannot be adequately described. Further, the "functional equivalents [thereof]" of the claimed invention are not adequately described to enable one of skill in the art to determine whether a given embodiment meets the

functional limitations that apply to the claimed subject matter, particularly since it is unclear what the "function" is.

Even if functional limitations were amended to recite "pesticidal effective" compositions comprising polynucleotides encoding a *particular* polypeptide (e.g. encoding SEQ ID Nos 1 or 2) affecting trypsin biosynthesis and/or egg development, there is no evidence of record that Applicants possess any pesticidal effective compositions according to the elected invention or that Applicants have provided an enabling disclosure teaching one how to make a pest control agent comprising a pesticidal effective amount of cells comprising a polynucleotide expressing a sufficient amount of bioactive NPF polypeptide. It is not at all clear what on what basis Applicants assert that the broad scope of claimed NPF embodiments can be used in methods for controlling the broad range of pests recited in the instant claims. Although Cerstiaens characterized the prior art as consistent with a *possible role* in insect reproduction for peptides of the superfamily of the FaRPs which includes the specific NPF polypeptides of the instant invention (SEQ ID NOs:1 and 2), it should be emphasized that at the time this invention was filed, "no effect *in vivo* from members of this extended family of peptides ha[d] been reported" (p. 40, middle, left column). Skilled artisans will recognize, for example, the difficulties in predicting *a priori* whether a given peptide can exhibit *any* functional activity in a non-native species. Preferred embodiments of the claimed invention are "exemplified [by] NPF polypeptides comprising an amino acid sequence selected from the group consisting of Ala-Arg-Gly-Pro-Gln-Leu-Arg-Leu-Arg-Phe-amide (SEQ ID NO.1) and Ala-Pro-Ser-Arg-Leu-Arg-Phe-

amide (SEQ ID NO.2)" (p. 5, lines 19-21). These peptides, alternatively designated as NPF I and NPF II, respectively (p. 5, line 12), are identical to the two peptides isolated from Colorado Potato Beetle brains which were originally described in a report by Spittaels et al. (Insect Biochem. Mol. Biol., 26(4):375-382, 1996; ref. AR in IDS filed 9/9/00). Spittaels noted that the invertebrate NPF-related peptides differ from the related NPY-family of vertebrate peptides in having a C-terminal amidated phenylalanine residue instead of the tyrosine residue that is observed in NPY-family members (sentence abridging left and right columns, p. 375) and further noted that "NPFs may occur both in extended forms (probably between 30 and 39 residues) and in shorter (truncated?) forms such as octa- or decapeptides...[as] seen in Octopus" (p. 380). Brown teaches that "NPY, PYY, PP, and NPF constitute a large superfamily of peptides...[wherein] [a]uthentic family members are 36 to 40 amino acids in length [and] *all are amidated*" (emphasis added; p. 1040, Brown et al., Peptides, 20:1035-1042, 1999). The importance of amidation to peptide bioactivity is underscored by the teachings of Merkler and Eipper et al. Merkler reported that "[s]tructure-activity data for 45 bioactive peptides show that the C-terminal amide is required for the full biological activity of most amidated peptide hormones (Enzyme Microb. Technol., 16:450-456, 1994; see abstract). Eipper teaches that for many peptides, "the presence of the α-amide moiety is essential for biological activity (Annu. Rev. Neurosci., 15:57-85, 1992; see p. 59, middle paragraph). Amidation is thought to provide "a role in protecting peptides from enzymatic degradation (half-life) and increasing binding affinity" (Eipper, p. 59, next-to-last paragraph). The only working example demonstrating a

biological effect for an NPF polypeptide in the specification (over the prior art) was in an assay in which mosquitos were injected with amidated peptides, NPF I and NPF II, which consisted of the primary amino acid sequences designated by SEQ ID NOs:1 and 2, respectively (Figs. 1 and 2), amidated peptides. These experiments showed that injections of NPF I and NPF II in mosquitos after a blood meal resulted in an inhibition of trypsin biosynthesis. The last paragraph on p. 23 describes a similar experiment which resulted in an inhibition in trypsin biosynthesis that was interpreted as suggesting that NPF I affect trypsin biosynthesis in the gut by binding to a TMOF receptor an not by the release of neuroendocrine factors from the brain or the thoracic ganglia that in turn release TMOF from the ovary" (p. 23, lines 27-29). It is further suggested that "[b]ecause the structure of NPF I is different from TMOF it appears that NPF I does not bind to TMOF specific binding site on the gut receptor but to a different site on the same or different receptor. However, analysis of described method does not allow one to conclude that NPF I binds to *any* receptor at all, nor are there any controls recited which would refute the notion that injection of large amounts of any peptide can result in inhibition of trypsin biosynthesis. More this sole working example of NPF peptide activity in mosquitos can hardly be construed as indicating that NPF I and/or II can control the broad range of pests recited in the instant claims. For one thing, inhibition of trypsin biosynthesis following administration of a *one particular pair* of Colorado Potato Beetle brain-derived *peptides* is not synonymous with controlling a broad range of pests via application to pest-inhabited loci of cells comprising a *polynucleotide* encoding an NPF polypeptide. In fact, in contrast to the intended effect of preventing egg development in

an insect pest, Cerstiaens recently demonstrated that NPF I actually *stimulated ovarian development* in locusts, but not in flies (p. 39, abstract). On the other hand, NPF II was reported to be far less gonadostimulatory agent than NPF I. Cerstiaens points out that "[t]he mode of action of Led-NPF 1 [i.e. NPF I] is as yet unknown." (p. 43, left column).

In vivo application of neuropeptides, let alone ingestion of cell material comprising polynucleotides encoding neuropeptides, is an unpredictable and unproven art. Rao reported that "neuropeptides have not been applied so far because it is believed that they would be rapidly degraded in the insect gut, due to their peptidic nature" (p. 1, left column, Gene, 175:1-5, 1996). However, despite allusions to other published data indicating that orally administered peptides may penetrate the insect gut and that undegraded fractions target haemocoelic cells and enter the haemolymph intact, Rao discloses that "there are no published data on the practical application of neuropeptides" (p. 1, right column). Skilled artisans will recognize that most neuropeptides are produced from larger precursors that undergo multiple, sequential post-translational processing steps, including amidation, which is typically a rate-limiting step requiring an amidating enzyme, peptidylglycine α-amidating monooxygenase (PAM), which in turn requires a precursor substrate (for α-amidation) consisting of the peptide stretch, -X-Gly-Basic-Basic- or occasionally -X-Gly-Basic (Eipper, p. 60, top paragraph and p. 78, middle paragraph). Apart from delivery and expression of pesticidal effective concentrations of NPF polypeptides in the cells to be ingested by pests, there is a fundamental problem associated with the use of polynucleotides comprising synthetic NPF genes for expression in food cells of amidated NPF: the specification does not

teach, with a reasonable expectation of success how to design an expression vector that *can* express an amidated NPF polypeptide, as exemplified by NPF I and II of the claimed invention, nor is there any reasonable expectation of success for the use of polynucleotides encoding NPF I, NPF II (or any other NPF polypeptides), as disclosed in the instant application, for any method of pest control management. Menn and Borkovec reported that "[i]f , as generally accepted, the biosynthesis of an insect neuropeptide is governed by a single encoding gene, it should be possible to clone a targeted gene and insert it via an appropriate vector for expression in an insect host, plant, or microbe. Although this is an attractive tactic, major obstacles are likely to be encountered including instability of expression in the host, instability of the site of expression in the host, rapid degradation in the transgenic host, and lack of appropriate processing enzymes in the host cell if the gene message is to synthesize the proneurohormone" (p. 278, left column, J. Agric. Food Chem., 37:271-278, 1989)..."A neuropeptide gene placed behind a string non-essential viral promoter is capable of turning an infected cell into a neuropeptide factory within the insect if the neuropeptide gene retains stability in the virus vector and if cellular processing and transport will mimic the activities of neuroendocrine tissue" (p. 278, right column). Indeed, the levels of amidating enzyme, PAM, whose activity is largely restricted to endocrine tissues, are highest in the central nervous system, especially the hypothalamus. With respect to the use of NPF I and II and its amidation in the claimed invention, however, there is no evidence of record suggesting *any* amidation activity to reside either in any of the recited insect food cells, especially in algae, Chlorella species, and yeast cells (as per claims 15-17 and 50-52), or in the highly acidic

gastrointestinal tract. Amidation has not been observed in procaryote or lower eukaryote. Furthermore, the specification fails to provide an enabling disclosure teaching to design polynucleotides that are capable of expressing pesticidal effective concentrations of biologically active NPF peptides. For one thing, expression of 2 to 5 amino acid polypeptides is not routinely practiced in the art (e.g. as per claim 7). More importantly, even if there amidation activity to post-translationally modify the expressed peptide, there is no written disclosure of *any* polynucleotide that can even *theoretically* express an amidated C-terminal phenylalanine residue or an N-terminal carboxylated, non-methionine residue (note: NPF I and II lack N-terminal methionines); none of the disclosed sequences carry the peptide sequence substrates required either for C-terminal amidation (i.e. glycine followed by one or two basic residues) or for N-terminal carboxylation (i.e. gamma carboxylation requires). Skilled artisans would recognize that N-terminal carboxylation (e.g. gamma carboxylation) of bioactive peptide substrates requiring N-terminal glutamic acid residues (generated by posttranslational cleavage) wherein there are no *a priori* rules governing effective substrate specificities. On the other hand, there is no reason to suggest from the prior art or the working examples that any of the recited NPF polypeptides of the disclosed invention would in fact be functional if they *were* carboxylated on the N-terminal ends. Moreover, like amidation, post-translational carboxylation modifications are similarly restricted according to tissue and host (which may or may not contain such an activity).

The inability to provide an enabling disclosure for making and using polynucleotide compositions expressing NPF I and II is underscores the lack of enablement for the broader scope of embodiments drawn to other NPF polypeptides, including analogues, derivatives or other functional equivalents to NPF I and II. As shown in the prior art revealing the gonadostimulatory properties of NPF I and II in locusts, there is a high degree of unpredictability associated with the use of the claimed embodiments, not only with respect to their activities in untested hosts, but also with respect to modified analogues or derivatives. In discussing peptide hormones, Rudinger has stated that "[t]he significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted a priori but must be determined from case to case by painstaking experimental study" (p. 6, 2nd to last sentence *In* J.A. Parsons, ed., "Peptide hormones", University Park Press, 1976). The Applicant has not taught how to make or use any other polynucleotide embodiments apart from those asserted to encode pesticidal effects on account of expression of biologically active NPF I and II. This especially the case given the lack of functional information concerning NPF I and II and its receptor. The specification does not teach which "particular" amino acid changes can be made among members of the NPF genus, especially since neither the prior art, nor the working examples shed any clear light teaching what the role of insect NPF polypeptides is, let alone a relatively uncharacterized pair of Colorado Potato Beetle brain-derived peptides. The unpredictability of the disclosed invention is further underscored by the absence of information concerning the stability of the claimed NPF polypeptides in the highly acidic gut which is loaded with proteolytic enzymes. The issue of

peptide stability and absorption is particularly pronounced in the desired case of generating pesticidal effective peptide levels in insects via ingestion of cellular food material comprising NPF-encoding polynucleotides. The clinical development of orally active peptide drugs has been restricted by their unfavorable physicochemical properties, which limit their intestinal mucosal permeation and their lack of stability against enzymatic degradation (Pauletti et al., J. Contolled Rel., 41:3-17, 1996; see abstract). Duve et al. (WO 95/24423) have described vector systems comprising a DNA sequence encoding an insect neuropeptide and a prolylhyroxylase enzyme to confer enhanced stability to the expressed peptide (see paragraph abridging p. 4-5). However, the instant specification fails to provide similar (or specific) guidance addressing the issues of peptide stability and does not provide examples of approaches to this problem that are routinely performed in the art (especially since there are none). Moreover, there is no evidence to suggest that Colorado Potato Beetle *brain-derived* peptides are stable to any appreciable extent in the guts of mosquitos, for example.

Apart from the question of whether NPF polypeptides of the claimed invention are stable in the gut, the specification does not provide clear guidance on how to make and use *polynucleotides to express* small peptides, as exemplified by NPF I and II. This is not routinely performed in the art. In one of the few reports where such an attempt was undertaken, Rao et al. (Gene, 1996) described tobacco plants transformed with expression constructs containing a multimerized coding region with six proctolin insect peptide units separated by putative arg-arg proteolytic cleavage sites. Part of the reason why primary translational products are not initially

synthesized as small 8-10 amino acid peptides is because small peptides are extremely unstable and susceptible to proteolytic digestion. Rao explained their choice of proctolin as a model peptide because "[i]t one of the best studied invertebrate neuropeptides...[because] its biologically active form is not amidated in its C-terminus nor blocked at its N terminus...[and based on] evidence indicating that proctolin permeates the larval gut and can be orally active" (p. 2, left column). There are no such analogous features ascribed to NPF I and II, nor does the specification provide a reasonable expectation of success for any method of controlling a pest, particularly since no one has *ever* reported the successful use of "ex vivo gene suicide" in the "control" of pests. It should also be noted that the specification provides no guidance teaching a way for polynucleotides to be used in the context of the claimed invention for expressing NPF polypeptides comprising dextrorotary or non-classical amino acids.

The physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fisher,* 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Given the unpredictable and undeveloped state of the art as described above, it would likely require considerable experimentation to appropriately develop the claimed invention for controlling pest comprising the use of polynucleotides expressing NPF polypeptides.

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed invention. This is particularly true given the state of the art, the nature of the invention, the unpredictability of the art, the scarcity of guidance and working examples in the specification, and the amount of experimentation necessary.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 14-64, 66-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 1 (and dependent claims) is incomplete since the method steps do not clearly relate back to the preamble which recites "[a] method of controlling a pest", since there is no mention in the method steps of "controlling a pest" nor in relating how expression of said polypeptide or functional equivalent "control[s] pest[s]". Moreover, it is unclear how "controlling" is defined in relation to "pest" or how application of an agent to a pest-inhabited locus controls pests.

Claims 1-10, 14-64, 66-70 are indefinite in their recitation of "NPF polypeptide" since it is unclear what embodiments are embraced by this term. The subject invention is said to involve the use of a polypeptide comprising an NPF peptide to control pest. "Specifically exemplified are NPF polypeptides comprising...SEQ ID NO. 1...SEQ ID NO. 2...[and] [i]n a preferred mode, the NPF polypeptides comprise an amino acid sequence which consists of a native NPF peptide or a fragment, analogue, derivative or other functional equivalent of an NPF peptide". This definition is unclear, since it fails to clearly define the structural limitations for any of the NPF polypeptides beyond those comprising the sequences of SEQ ID NOs. 1 or 2. Furthermore, it is unclear what "NPF" means in the context of the recited embodiments, since there are no recited embodiments which possess the sequence "NPF". Moreover, the disclosure fails to disclose whether recitation of "functional equivalent of an NPF peptide" in the alternative applies to any of the members of the group consisting of "fragment", "analogue" or "derivative" or what constitutes a "functional equivalent" in the context of the claim, particularly since neither the term nor function is defined. Additionally, the claims are indefinite in their recitation of "functional equivalent[s] [thereof]" since it is not unclear how this phrase is defined or what it refers to since it is unclear what the "function" is.

Claims 14, 40 and 49 are indefinite in its recitation of "optimized for expression" since it is unclear how this phrase is defined in the context of the claim, particularly there are no method steps or structural limitations associated with said phrase.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

Joe Woitach
AU1632